CLAIMS

1. A derivative of an antibody, comprising a monoclonal antibody or the antibody fragment thereof which specifically reacts with ganglioside GD3 which is conjugated with a radioisotope, a protein or a low molecular weight agent.

2. The derivative of an antibody according to claim 1, wherein the monoclonal antibody which specifically reacts with ganglioside GD3 is an antibody selected from an antibody produced by a hybridoma, a humanized antibody and a human antibody.

3. The derivative of an antibody according to claim 1 or 2, wherein the monoclonal antibody comprises CDR1, CDR2 and CDR3 of H chain V region having the amino acid sequences represented by SEQ ID NOs:3, 4 and 5, respectively.

4. The derivative of an antibody according to claim 1 or 2, wherein the monoclonal antibody comprises CDR1, CDR2 and CDR3 of L chain V region having the amino acid sequences represented by SEQ ID NOs:6, 7 and 8, respectively.

5. The derivative of an antibody according to claim 1 or 2, wherein the monoclonal antibody comprises:

CDR1, CDR2 and CDR3 of a heavy chain (H chain) variable region (V region) having the amino acid sequences represented by SEQ ID NOs:3, 4 and 5, respectively; and

CDR1, CDR2 and CDR3 of a light chain (L chain) V region having the amino acid sequences represented by SEQ ID NOs:6, 7 and 8, respectively.

6. The derivative of an antibody according to claim 2, wherein the antibody produced by a hybridoma is KM641 (FERM BP-3116).

7. The derivative of an antibody according to claim 2, wherein the humanized antibody is a human chimeric antibody or a human CDR-grafted antibody.

8. The derivative of a human chimeric antibody according to claim 7, wherein the human chimeric antibody comprises an H chain V region and an L chain V region of a monoclonal antibody against ganglioside GD3 produced by a hybridoma.

9. The derivative of a human chimeric antibody according to claim 7, wherein the human chimeric antibody comprises:

an H chain V region and an L chain V region of a monoclonal antibody produced against ganglioside GD3 by a hybridoma; and

an H chain constant region (C region) and an L chain C region of a human antibody.

10. The derivative of a human chimeric antibody according to claim 8 or 9, wherein the H chain V region comprises the amino acid sequence represented by SEQ ID NO:55.

11. The derivative of a human chimeric antibody according to claim 8 or 9, wherein the L chain V region comprises the amino acid sequence represented by SEQ ID NO:56.

12. The derivative of a human chimeric antibody according to claim 8 or 9, wherein

the H chain V region comprises the amino acid sequence represented by SEQ ID NO:55; and

the L chain V region comprises the amino acid sequence represented by SEQ ID NO:56.

a3 13. The derivative of a human chimeric antibody KM871 according to claim 8 or 9, wherein

the H chain V region comprises the amino acid sequence represented by SEQ ID NO:55; and

the L chain V region comprises the amino acid sequence represented by SEQ ID NO:56.

14. The derivative of a human CDR-grafted antibody according to claim 7, wherein the human CDR-grafted antibody comprises CDR of an H chain V region and an L chain V region of a monoclonal antibody against ganglioside GD3.

15. The derivative of a human CDR-grafted antibody according to claim 7, wherein the human CDR-grafted antibody comprises:

CDRs of an H chain V region and an L chain V region of a monoclonal antibody against ganglioside GD3; and

framework regions (FRs) of an H chain V region and an L chain V region of a human antibody.

16. The derivative of an antibody according to claim 7, wherein the human CDR-grafted antibody comprises:

CDRs of an H chain V region and an L chain V region of a monoclonal antibody against ganglioside GD3;

FRs of an H chain V region and an L chain V region of a human antibody; and

an H chain C region and an L chain C region of a human antibody.

17. The derivative of a human CDR-grafted antibody according to any one of claims 14 to 16, wherein the antibody comprises CDR1, CDR2 and CDR3 of the H chain V region having the amino acid sequences represented by SEQ ID NOs:3, 4 and 5, respectively.

18. The derivative of a human CDR-grafted antibody according to any one of claims 14 to 16, wherein the antibody comprises CDR1, CDR2 and CDR3 of the L chain V region having the amino acid sequences represented by SEQ ID NOs:6, 7 and 8, respectively.

19. The derivative of a human CDR-grafted antibody according to any one of claims 14 to 16, wherein the antibody comprises:

CDR1, CDR2 and CDR3 of the H chain V region having the amino acid sequences represented by SEQ ID NOs:3, 4 and 5, respectively; and

CDR1, CDR2 and CDR3 of the L chain V region having the amino acid sequences represented by SEQ ID NOs:6, 7 and 8, respectively.

20. The derivative of a human CDR-grafted antibody according to any one of claims 14 to 16, wherein the H chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:9.

21. The derivative of a human CDR-grafted antibody according to any one of claims 14 to 16, wherein the L chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:54.

22. The derivative of a human CDR-grafted antibody according to any one of claims 14 to 16, wherein the H chain V region and the L chain V region of the antibody

comprises the amino acid sequences represented by SEQ ID NO:9 and SEQ ID NO:54, respectively.

23. The derivative of a human CDR-grafted antibody KM8871 according to any one of claims 14 to 16, wherein

the H chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:9; and

the L chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:54.

24. The derivative of the antibody fragment according to claim 1, wherein the antibody fragment is an antibody fragment selected from Fab, Fab', $F(ab')_2$, a single chain antibody (scFv), a disulfide stabilized V region fragment (dsFv) and a peptide comprising CDR.

25. The derivative of the antibody fragment according to claim 1 or 24, wherein the antibody fragment comprises amino acid sequences of an H chain V region and an L chain V region of a monoclonal antibody against ganglioside GD3 produced by a hybridoma.

26. The derivative of the antibody fragment according to claim 1 or 24, wherein the antibody fragment comprises an H chain V region of the antibody having the amino acid sequence represented by SEQ ID NO:55.

27. The derivative of the antibody fragment according to claim 1 or 24, wherein the antibody fragment comprises an L chain V region of the antibody having the amino acid sequence represented by SEQ ID NO:56.

28. The derivative of the antibody fragment according to claim 1 or 24, wherein the antibody fragment comprises:

an H chain V region of the antibody having the amino acid sequence represented by SEQ ID NO:55; and

an L chain V region of the antibody having the amino acid sequence represented by SEQ ID NO:56.

29. The derivative of the antibody fragment according to claim 1 or 24, wherein the antibody fragment comprises amino acid sequences of an H chain V region and an L chain V region of a human CDR-grafted antibody against ganglioside GD3.

30. The derivative of the antibody fragment according to claim 1 or 24, wherein the antibody fragment comprises an H chain V region of the antibody having the amino acid sequence represented by SEQ ID NO:9.

31. The derivative of the antibody fragment according to claim 1 or 24, wherein the antibody fragment comprises an L chain V region of the antibody having the amino acid sequence represented by SEQ ID NO:54.

32. The derivative of the antibody fragment according to claim 1 or 24, wherein the antibody fragment comprises:

an H chain V region of the antibody having the amino acid sequence represented by SEQ ID NO:9; and

an L chain V region of the antibody having the amino acid sequence represented by SEQ ID NO:54.

33. The derivative of an antibody fragment according to claim 1 or 24, wherein the antibody fragment comprises CDR1, CDR2 and CDR3 of an H chain V region of the antibody having the amino acid sequences represented by SEQ ID NOs:3, 4 and 5, respectively.

34. The derivative of the antibody fragment according to claim 1 or 24, wherein the antibody fragment comprises CDR1, CDR2 and CDR3 of an L chain V region of the antibody having the amino acid sequences represented by SEQ ID NOs:6, 7 and 8, respectively.

35. The derivative of the antibody fragment according to claim 1 or 24, wherein the antibody fragment comprises:

CDR1, CDR2 and CDR3 of an H chain V region of the antibody having the amino acid sequences represented by SEQ ID NOs:3, 4 and 5; and

CDR1, CDR2 and CDR3 of an L chain V region of the antibody having the amino acid sequences represented by SEQ ID NOs:6, 7 and 8.

36. The derivative of a monoclonal antibody or the antibody fragment thereof according to any one of claim 1 to 35, wherein the protein is a cytokine.

37. The derivative of a monoclonal antibody or the antibody fragment thereof according to claim 36, wherein the cytokine is human interleukin-2 (hIL-2).

38. The derivative of an antibody according to claim 37, wherein the derivative of an antibody comprises a human chimeric antibody KM871 and hIL-2.

39. The derivative of an antibody according to claim 38, wherein the antibody conjugated with hIL-2 comprises:

an H chain V region having the amino acid sequence represented by SEQ ID NO:57; and

an L chain V region having the amino acid sequence represented by SEQ ID NO:56.

40. The derivative of an antibody according to claim 37, wherein the derivative of an antibody comprises a human CDR-grafted antibody KM8871 and hIL-2.

41. The derivative of an antibody according to claim 1, wherein the antibody conjugated with hIL-2 comprises:

an H chain V region having the amino acid sequence represented by SEQ ID NO:53; and

an L chain V region having the amino acid sequence represented by SEQ ID NO:54.

42. A DNA which encodes the derivative of a monoclonal antibody or the derivative of the antibody fragment thereof which specifically reacts with ganglioside GD3 according to any one of claims 1 to 41.

43. A recombinant vector comprising the DNA according to claim 42.

44. A transformant which is obtained by introducing the recombinant vector according to claim 43 into a host cell.

45. A transformant KM871hIL2 (FERM BP-6918) which produces the antibody according to claim 38.

46. A transformant KM8871hIL2 (FERM BP-6791) which produces the antibody according to claim 40.

47. A process for producing an antibody, which comprises:

culturing the transformant according to any one of claims 44 to 46 in a culture medium to produce and

accumulate the derivative of a monoclonal antibody or the derivative of the antibody fragment thereof according to any one of claims 1 to 41 in the culture; and

recovering the derivative of the antibody or the derivative of the antibody fragment thereof from the culture.

48. A human CDR-grafted antibody or the antibody fragment thereof which specifically reacts with ganglioside GD3.

49. The human CDR-grafted antibody or the antibody fragment thereof according to claim 48, wherein the human CDR-grafted antibody comprises CDRs of an H chain V region and an L chain V region of a monoclonal antibody against ganglioside GD3.

50. The human CDR-grafted antibody or the antibody fragment thereof according to claim 48, wherein the human CDR-grafted antibody comprises:

CDRs of an H chain V region and an L chain V region of a monoclonal antibody against ganglioside GD3; and

FRs of an H chain V region and an L chain V region of a human antibody.

51. The human CDR-grafted antibody or the antibody fragment thereof according to claim 48, wherein the human CDR-grafted antibody comprises:

CDRs of an H chain V region and an L chain V region of a monoclonal antibody against ganglioside GD3;

FRs of an H chain V region and an L chain V region of a human antibody; and

an H chain C region and an L chain C region of a human antibody.

52. The human CDR-grafted antibody or the antibody fragment thereof according to any one of claims 49 to 51, wherein the antibody comprises CDR1, CDR2 and CDR3 of the H chain V region having the amino acid sequences represented by SEQ ID NOs:3, 4 and 5, respectively.

53. The human CDR-grafted antibody or the antibody fragment thereof according to any one of claims 49 to 51, wherein the antibody comprises CDR1, CDR2 and CDR3 of the L chain V region having the amino acid sequences represented by SEQ ID NOs:6, 7 and 8, respectively.

54. The human CDR-grafted antibody or the antibody fragment thereof according to any one of claims 49 to 51, wherein the antibody comprises:

CDR1, CDR2 and CDR3 of the H chain V region having the amino acid sequences represented by SEQ ID NOs:3, 4 and 5, respectively; and

CDR1, CDR2 and CDR3 of the L chain V region having the amino acid sequences represented by SEQ ID NOs:6, 7 and 8.

55. The human CDR-grafted antibody or the antibody fragment thereof according to any one of claims 49 to 51, wherein the H chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:9.

56. The human CDR-grafted antibody or the antibody fragment thereof according to any one of claims 49 to 51, wherein the L chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:54.

57. The human CDR-grafted antibody or the antibody fragment thereof according to any one of claims 49 to 51, wherein

the H chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:9; and

the L chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:54.

58. The human CDR-grafted antibody KM8871 or the antibody fragment thereof according to any one of claims 49 to 51, wherein

the H chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:9; and

the L chain V region of the antibody comprises the amino acid sequence represented by SEQ ID NO:54.

59. A DNA which encodes the human CDR-grafted antibody or the antibody fragment thereof which specifically reacts with ganglioside GD3 according to any one of claims 48 to 58.

60. A recombinant vector comprising the DNA according to claim 59.

61. A transformant which is obtained by introducing the recombinant vector according to claim 60 into a host cell.

62. A transformant KM8871 (FERM BP-6790) which produces the human CDR-grafted antibody according to claim 58.

63. A process for producing an antibody, which comprises:

culturing the transformant according to claim 61 or 62 in a culture medium to produce and accumulate the human CDR-grafted antibody or the antibody fragment thereof according to any one of claims 48 to 58 in the culture; and

recovering the antibody or the antibody fragment thereof from the culture.

64. A medicament comprising at least one selected from the derivative of a monoclonal antibody and the derivative of the antibody fragment thereof according to claims 1 to 41 and the human CDR-grafted antibody and the antibody fragment thereof according to any one of claims 48 to 58.

a9 65. A therapeutic agent for cancers, comprising, as an active ingredient, at least one selected from the derivative of a monoclonal antibody and the derivative of the antibody fragment thereof according to any one of claims 1 to 41 and the human CDR-grafted antibody and the antibody fragment thereof according to any one of claims 48 to 58.

66. A diagnostic agent for cancers, comprising, as an active ingredient, at least one selected from the derivative of a monoclonal antibody and the derivative of the antibody fragment thereof according to any one of claims 1 to 41 and the human CDR-grafted antibody and the antibody fragment thereof according to any one of claims 48 to 58.